

CARDIOVASCULAR MEDICINE

Acute improvement of atrial mechanical stunning after electrical cardioversion of persistent atrial fibrillation: comparison between biatrial and single atrial pacing

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Objective: To evaluate the acute effects of atrial pacing at different pacing sites on mechanical stunning after cardioversion of atrial fibrillation (AF).

Setting: Tertiary referral centre.

Patients: 20 patients with persistent AF were studied.

Interventions: Spontaneous echo contrast (SEC), left atrial appendage emptying velocity (LAAEV), and left atrial appendage emptying fraction (LAAEF) were assessed by transoesophageal echocardiography (TOE) during AF, after conversion to sinus rhythm, and during atrial pacing from the right atrial appendage, left lateral atrium, and both atria simultaneously. Transmitral inflow velocity of the atrial wave (TMIF-A) by TOE and the maximum P wave duration in 12 lead ECG were also measured during sinus rhythm and atrial pacing.

Main outcome measures: Comparison of atrial mechanical function and P wave duration in 12 lead ECG during atrial pacing from different sites after cardioversion of AF.

Results: Compared with sinus rhythm, atrial pacing at 80 beats/min increased LAAEV from mean (SD) 14.6 (10.1) to 33.4 (19.8) cm/s ($p = 0.001$), LAAEF from 13.8 (8.5) to 32.1 (11.2)% ($p < 0.001$), and TMIF-A from 24.6 (11.9) to 45.6 (21.0) cm/s ($p < 0.001$) and reduced SEC grade from 2.6 (1.0) to 1.6 (0.9) ($p < 0.001$). These effects had a positive force–frequency relation. Biatrial pacing produced the shortest P wave duration and resulted in the most significant improvement in atrial function (LAAEV, 33.2 (19.3) v 53.7 (23.9) cm/s, $p = 0.0001$; LAAEF, 31.9 (11.1) v 46.2 (12.6)%, $p < 0.0001$; TMIF-A, 37.7 (18.3) v 54.1 (21.2) cm/s, $p < 0.001$; SEC grade, 1.4 (1.1) v 0.8 (0.9), $p = 0.001$, right atrial appendage versus biatrial pacing).

Conclusions: Atrial pacing at increased rates can improve atrial mechanical function after cardioversion of persistent AF. Biatrial pacing may be the most effective technique to reverse atrial mechanical stunning.

A transient decrease in atrial mechanical function, referred to as atrial mechanical stunning, is a well documented phenomenon after cardioversion of atrial fibrillation (AF).^{1–4} Atrial mechanical stunning is thought to be one of the mechanisms responsible for the increased risk of thromboembolic complications after cardioversion of AF.^{5,6} A number of transthoracic and transoesophageal echocardiography (TOE) studies have shown that after cardioversion the mechanical function of the left atrium and left atrial appendage (LAA) is reduced, resulting in lower LAA blood flow velocities, which in turn predisposes patients to the formation of new thrombi.^{1–12} The atrial mechanical stunning is thought to be related to the properties of the preceding arrhythmia rather than the mode of cardioversion and can be considered a form of tachycardia induced cardiomyopathy.¹³ Sanders and colleagues^{14,15} showed that atrial mechanical stunning after cardioversion of chronic atrial flutter and short duration AF can be reversed both by atrial pacing and through the administration of either isoproterenol or calcium. However, both the effects of atrial pacing and the effects of varying the pacing sites and rates on atrial stunning after cardioversion of AF have not been evaluated. This study aimed to determine, by using TOE, the acute effects of atrial pacing and the effects of varying the pacing sites and rates on atrial mechanical function just after electrical cardioversion of persistent AF.

METHODS

Patients

We studied 20 consecutive patients (13 men, mean (SD) age 57 (15) years) who had persistent AF between 3–6 months in

duration and underwent electrical cardioversion and TOE to rule out the presence of left atrial thrombi (table 1). All patients gave written informed consent to the study, which was approved by Clinical Research Ethics Committee of the Osaka City University.

All patients were treated with warfarin and controlled to have an international normalised ratio between 2–2.5 for three weeks before cardioversion. All antiarrhythmic drugs were continued before and after cardioversion.

Echocardiographic analysis

A viscous 2% lidocaine solution was used for oropharyngeal anaesthesia and propofol was used for sedation. TOE was recorded with a 6 MHz multiplane probe connected to an Acuson Sequoia ultrasound system (Acuson Corporation, Mountain View, California, USA).

Before cardioversion, LAA was scanned in planes to establish the angle for obtaining maximum LAA areas. The mitral valve was also scanned on a four chamber image to establish the angle at which the maximum transmitral flow could be obtained. During cardioversion, the probe was left in place and the echocardiograph disconnected. After cardioversion, the resultant angles were used for subsequent analysis.

LAA emptying velocity (LAAEV) was assessed by pulsed Doppler echocardiography by placing the sample volume

Abbreviations: AF, atrial fibrillation; LAA, left atrial appendage; LAAEF, left atrial appendage emptying fraction; LAAEV, left atrial appendage emptying velocity; RAA, right atrial appendage; SEC, spontaneous echo contrast; TMIF-A, transmitral inflow velocity of the atrial wave; TOE, transoesophageal echocardiography

Table 1 Characteristics of patients with persistent atrial fibrillation

Patient number	Age (years)	Sex	Associated heart disease	Duration of AF (months)	LVEF (%)	Left atrial diameter (mm)	SEC grade during AF	Sinus rate after cardioversion (beats/min)
1	70	F	None	3	56	44	1	70
2	51	M	HHD	5	55	49	2	38
3	74	M	None	3	59	35	1	66
4	46	M	DCM	4	42	42	1	72
5	76	F	None	3	64	52	2	41
6	58	M	None	3	58	41	1	76
7	77	M	DCM	3	25	52	4	73
8	58	M	HHD	3	44	38	1	66
9	53	F	DCM	5	37	55	2	72
10	58	F	OMI	3	31	53	1	41
11	17	M	None	6	57	39	0	78
12	51	M	None	6	70	38	0	76
13	67	M	DCM	6	28	47	3	75
14	34	M	None	3	60	43	1	74
15	62	F	None	3	55	46	4	64
16	48	M	HCM	3	55	50	1	62
17	52	M	HHD	5	65	40	0	70
18	68	F	OMI	3	42	49	1	48
19	56	F	None	4	62	38	0	76
20	70	M	DCM	5	32	52	2	55

AF, atrial fibrillation; DCM, dilated cardiomyopathy; F, female; HCM, hypertrophic cardiomyopathy; HHD, hypertensive heart disease; LVEF, left ventricular ejection fraction; M, male; OMI, old myocardial infarction; SEC, spontaneous echo contrast.

1.5 cm into the entrance of the LAA. Maximum and minimum LAA areas were measured by planimetry, and LAA emptying fraction (LAAEF) was calculated from the formula $LAAEF = (\text{maximum LAA area} - \text{minimum LAA area}) / \text{maximum LAA area}$. Left atrial function was assessed from pulsed Doppler interrogation of transmitral inflow by

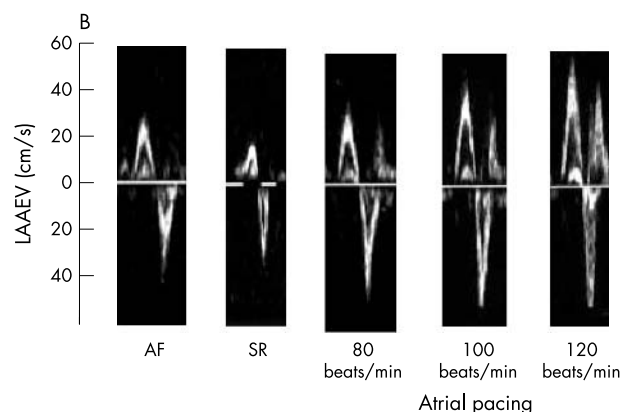
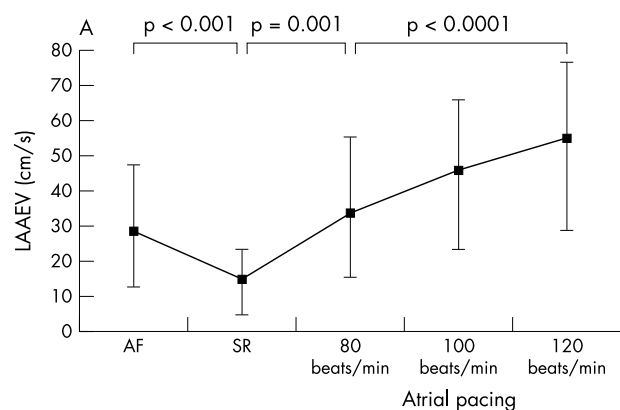


Figure 1 (A) Left atrial appendage emptying velocity (LAAEV) during atrial fibrillation (AF), sinus rhythm (SR) after cardioversion, and atrial pacing at 80, 100, and 120 beats/min. (B) Representative LAAEF.

placing the sample volume at the leaflet tips, and the transmitral inflow velocity of the atrial wave (TMIF-A) was measured.

Spontaneous echo contrast (SEC) was defined as dynamic intracavity echoes of a swirling pattern distinct from white noise artefact. Gain settings were sequentially reduced to exclude white noise artefact. The degree of SEC was graded from 0 to 4 according to previously published criteria¹⁶: 0, none (absence of echogenicity); 1+, mild (minimum echogenicity located in the LAA or sparsely distributed in the main cavity of the left atrium); 2+, mild to moderate (more dense swirling pattern than 1+ but with similar distribution); 3+, moderate (dense swirling pattern in the LAA, generally associated with somewhat lesser intensity in the main cavity); 4+, severe (intense echodensity and very slow swirling patterns in the LAA, usually with similar density in the main cavity).

These parameters were measured independently off line by two experienced observers. Three consecutive measurements taken during sinus rhythm after cardioversion and each atrial pacing were averaged. LAAEV, LAAEF, and SEC were also measured during AF, and six consecutive measurements were averaged.

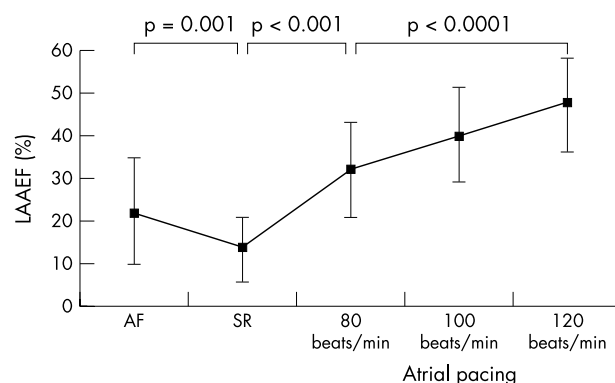


Figure 2 Left atrial appendage emptying fraction (LAAEF) during AF, SR after cardioversion, and atrial pacing at 80, 100, and 120 beats/min.

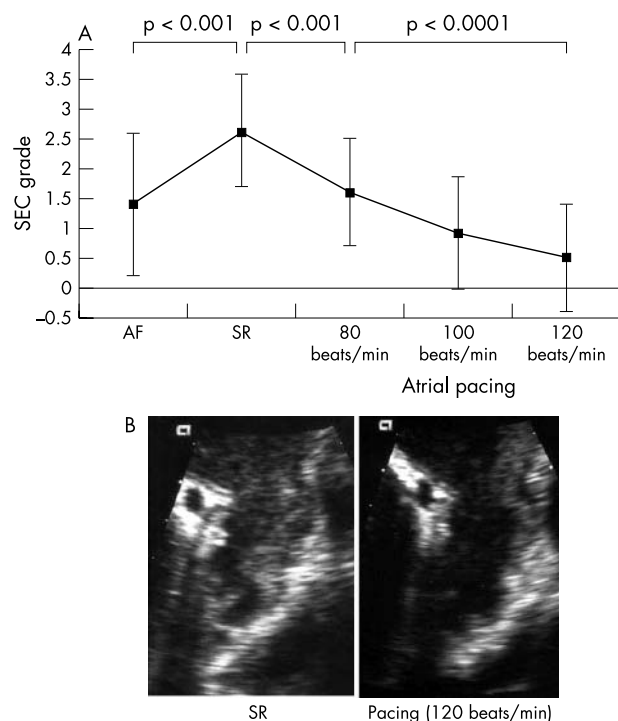


Figure 3 (A) Spontaneous echo contrast (SEC) grade during AF, SR after cardioversion, and atrial pacing at 80, 100, and 120 beats/min. (B) Representative SEC during SR and pacing at 120 beats/min.

Pacing protocol

Before the initial TOE evaluation during AF, a 6 French steerable quadripolar electrode catheter with 2.5 mm inter-electrode spacing (Steerocath Dx, EP Technologies Inc, San Jose, California, USA) was introduced percutaneously through the femoral vein and positioned in the right atrial appendage (RAA) under fluoroscopic guidance. A 5 French decapolar catheter with 2 mm interelectrode spacing (Torqr, Medtronic Inc, Minneapolis, Minnesota, USA) was placed into the left lateral site of the coronary sinus. After conversion to sinus rhythm, bipolar pacing at 80 beats/min presented in random order from the RAA, coronary sinus, and both atria simultaneously was performed at twice the diastolic threshold with a pulse duration of 2 ms delivered from a programmable stimulator (SEC-3120, Nihon Kohden, Tokyo, Japan). In 18 of 20 patients, who had no second degree atrioventricular blocks at 100 beats/min or 120 beats/min, also underwent randomly presented bipolar pacing at 100 beats/min and 120 beats/min from the RAA, coronary sinus, and both atria. Surface 12 lead ECG and intracardiac bipolar electrograms were filtered from 30 to 500 Hz and recorded on a computer based digital amplifier and recorder system with optical disk storage. The maximum P wave duration was measured with computer assisted calipers at a sweep speed of 200 mm/s. The onset of the P wave was defined as the point of the first visible upward departure of the trace from the bottom of the baseline for the positive waves and as the point of the first downward departure from the top of the baseline for negative waves. The return of the baseline to the bottom of the trace in positive waves and to the top of the trace in negative waves was considered to be the end of the P wave. Maximum P wave duration during pacing was determined as the duration from the pacing spike to the end of the P wave in the same lead where the maximum P wave duration was found during sinus rhythm.

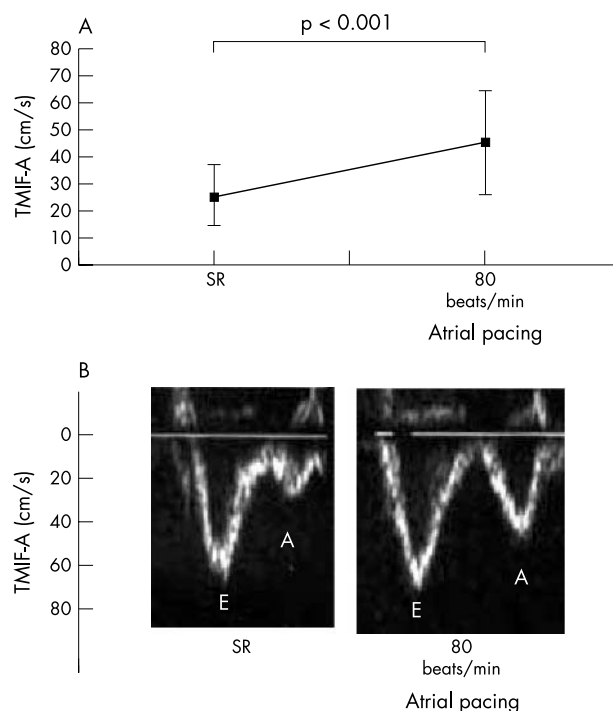


Figure 4 (A) Transmittal inflow velocity of the atrial wave (TMIF-A) during SR after cardioversion and atrial pacing at 80 beats/min. (B) Representative TMIF-A during SR and pacing at 80 beats/min. A, atrial filling wave; E, early filling wave.

Cardioversion protocol

After completion of the TOE measurements during AF, all patients underwent transthoracic electrical cardioversion under deep sedation. Sinus rhythm was restored by 100–200 J shocks in all patients. No patient was found to have either a left atrial thrombus or thromboembolic complications before and after cardioversion.

Study protocol

In all patients, LAAEV, LAAEF, and SEC were measured during AF, sinus rhythm after cardioversion, and atrial pacing from the RAA, coronary sinus, and both atria at 80 beats/min. TMIF-A was measured during sinus rhythm and atrial pacing. In 18 of 20 patients, LAAEV, LAAEF, and SEC were also measured during atrial pacing from the RAA, coronary sinus, and both atria at 100 beats/min and 120 beats/min to confirm a positive force–frequency relation.

These parameters were determined 10 minutes after conversion to sinus rhythm and 10 minutes after the start of atrial pacing from each site and at each rate. The interval between pacing was five minutes to avoid recording transitional results.

Statistical analysis

All variables are reported as mean (SD). Results during AF, sinus rhythm, and each atrial pacing at 80 beats/min, and the effects of pacing rate and pacing site were compared with nested analysis of variance with Scheffe's test. The inter-observer and intraobserver variability were assessed according to the Bland and Altman method. Values of $p < 0.05$ were considered significant.

RESULTS

Characteristics of patients with persistent AF

Of the 20 patients, five had dilated cardiomyopathy, three had hypertensive heart disease, two had previous myocardial infarction, one had hypertrophic cardiomyopathy, and the

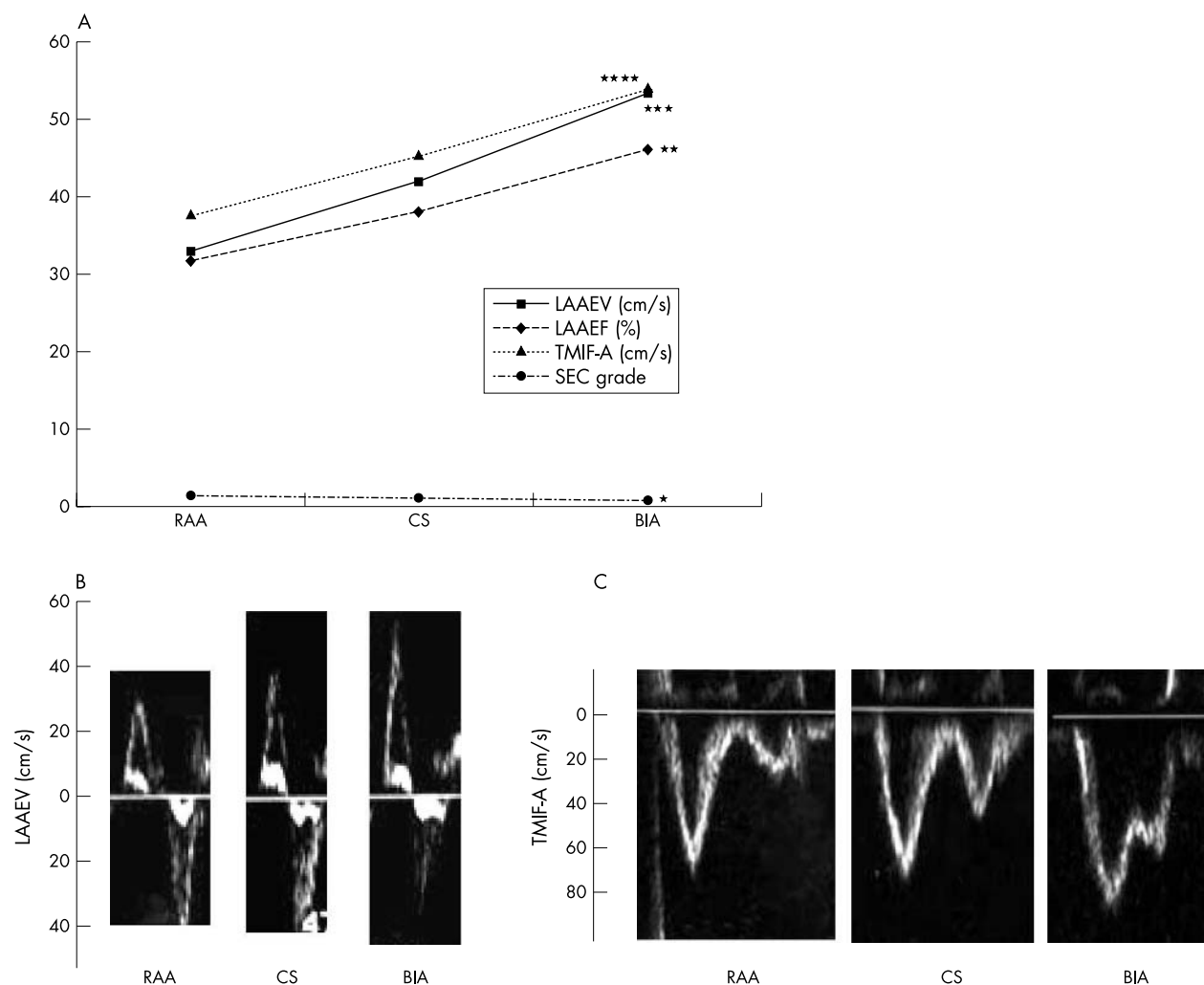


Figure 5 (A) Comparison of LAAEV, LAAEF, TMIF-A, and SEC between right atrial appendage (RAA), lateral coronary sinus (CS), and biatrial pacing (BIA). * $p=0.001$, ** $p<0.001$, *** $p=0.0001$, **** $p<0.0001$, RAA ν BIA. (B) Representative LAAEV. (C) Representative TMIF-A.

remaining nine had no structural heart disease (table 1). Mean (SD) left ventricular ejection fraction was 50.8 (13.3)% and left atrial size was 45.2 (6.1) mm. All patients were successfully cardioverted as defined by the maintenance of sinus rhythm. After cardioversion, sinus rates were under 80 beats/min (64.7 (13.0) beats/min) in all patients. No patient had an early AF relapse for about two hours after successful cardioversion during this study protocol. Before cardioversion, 16 of 20 patients (80%) were found to have SEC.

Atrial mechanical function during sinus rhythm after cardioversion of persistent AF

After cardioversion, LAAEV (fig 1) and LAAEF (fig 2) decreased compared with the pre-cardioversion value. LAAEV decreased from 28.4 (17.7) cm/s to 14.6 (10.1) cm/s ($p < 0.001$), whereas LAAEF decreased from 21.7 (12.0)% to 13.8 (8.5)% ($p = 0.001$).

After electrical cardioversion, new or increased SEC was detected in 18 of the 20 patients (90%). SEC grade increased from 1.4 (1.2) to 2.6 (1.0) ($p < 0.001$) (fig 3).

Effect of atrial pacing rate and site on atrial mechanical function

Compared with sinus rhythm, atrial pacing at 80 beats/min significantly increased LAAEV from 14.6 (10.1) cm/s to 33.4 (19.8) cm/s ($p = 0.001$) (fig 1), increased LAAEF from 13.8

(8.5)% to 32.1 (11.2)% ($p < 0.001$) (fig 2), increased TMIF-A from 24.6 (11.9) cm/s to 45.6 (21.0) cm/s ($p < 0.001$) (fig 4), and reduced SEC grade from 2.6 (1.0) to 1.6 (0.9) ($p < 0.001$) (fig 3). An increase in the atrial pacing rate resulted in significantly greater increases in LAAEV from 33.4 (19.8) cm/s to 55.0 (23.6) cm/s ($p < 0.0001$) and in LAAEF from 32.1 (11.2)% to 47.7 (11.4)% ($p < 0.0001$) at 80 beats/min ν 120 beats/min, respectively) (figs 1 and 2). Increased atrial pacing at 80 beats/min ν 120 beats/min also produced a significant reduction in the magnitude of SEC from 1.6 (0.9) to 0.5 (0.8) ($p < 0.0001$) (fig 3). Comparing between pacing sites, biatrial pacing resulted in the most significant improvement in atrial function (LAAEV, 33.2 (19.3) cm/s ν 53.7 (23.9) cm/s, $p = 0.0001$; LAAEF, 31.9 (11.1)% ν 46.2 (12.6)%, $p < 0.0001$; TMIF-A, 37.7 (18.3) cm/s ν 54.1 (21.2) cm/s, $p < 0.001$; SEC grade, 1.4 (1.1) ν 0.8 (0.9), $p = 0.001$, with RAA ν biatrial pacing) (fig 5). There was no significant difference in these parameters between RAA and coronary sinus pacing.

There was no significant difference in interobserver nor intraobserver variability.

Maximum P wave duration during sinus rhythm and atrial pacing

After conversion to sinus rhythm, all patients had prolonged P wave duration (135 (15) ms). There was no significant

change in the duration of the P wave between sinus rhythm, RAA pacing (141 (23) ms), and coronary sinus pacing (147 (38) ms). However, biatrial pacing resulted in a P wave with the shortest duration (102 (13) ms, $p < 0.001$).

DISCUSSION

Main findings

The present study provides new findings about atrial mechanical function in mechanically stunned atrium after cardioversion of persistent AF. Atrial pacing results in an acute improvement in atrial mechanical function just after cardioversion of persistent AF. This effect of atrial pacing has a positive force-frequency relation. The most significant improvement in atrial mechanical function was achieved by simultaneous biatrial pacing when compared with single site atrial pacing.

Atrial mechanical function after conversion to sinus rhythm

We observed a high incidence of stunned left atrial and LAA function after electrical cardioversion of persistent AF in agreement with previous reports.^{1–9} No significant difference in the incidence and severity of stunned atrial mechanical function after all modes of cardioversion of AF has been reported.^{3 7 13 17} Therefore, the decrease in LAAEV and LAAEF and new or increased SEC we describe in this study may be typical findings after conversion to sinus rhythm.

Effect of atrial pacing rate

It has been reported that ventricular contraction is greater with increasing heart rate in the normal heart, but not in the failing heart.¹⁸ The release of calcium from sarcoplasmic storage is thought to be the mechanism underlying the frequency dependent force generation.^{19 20} It remains unknown whether atrial mechanical function is influenced by an increased heart rate in the normal human heart. Agmon and colleagues²¹ reported a positive relation between heart rate and LAAEV, but patients with sinus tachycardia had a worse LAAEV. Sanders and colleagues^{14 15} showed in patients after cardioversion of chronic atrial flutter and short duration AF that LAAEV improved stepwise with an increased pacing rate at atrial cycle lengths between 750 ms and 500 ms. In the present study, we also observed a stepwise improvement in stunned LAA mechanical function with increased pacing rate after cardioversion of persistent AF. This suggests that in patients with atrial stunning after cardioversion of persistent AF, the atrial contractile apparatus is intact but functionally impaired and suggests also that atrial stunning is reversible and may be associated with a different mechanism that causes heart failure. Atrial mechanical dysfunction after atrial tachyarrhythmias is related to a diminished calcium transient,^{22–24} resulting from a reduction in L-type calcium current density.^{25 26} In the present study we suggest that increased intracellular calcium concentrations associated with increasing atrial pacing may improve atrial mechanical function and that a deficiency in intracellular calcium may be responsible for atrial stunning after cardioversion of persistent AF.

Effect of atrial pacing for global left atrial function

A previous report about the effect of pacing on atrial mechanical function was limited to the evaluation of LAA function.^{14 15} Agmon and colleagues²⁷ showed that LAAEV correlates poorly with global left atrial variables, indicating that LAAEV is inadequate to be used as a surrogate of global left atrial function. In the present study, we have shown that atrial pacing significantly increased TMIF-A. To the best of our knowledge, this is the first clinical report that atrial pacing can improve global left atrial function in the

mechanically stunned atrium after cardioversion of persistent AF.

Effect of atrial pacing site

Recently, it has been shown that biatrial pacing can be more effective than standard RAA pacing in reducing the recurrence of AF.^{28–32} Acute electrophysiological studies have suggested that a reduction in the atrial conduction delay by simultaneous activation of both atria is an important mechanism of improved prevention of AF.^{28 29 31 33 34} The effects of alternate and multisite atrial pacing on atrial stunning after cardioversion of AF have yet to be evaluated. In the present study biatrial pacing produced a significant improvement in atrial mechanical function after cardioversion of persistent AF in comparison with single site (RAA or coronary sinus) atrial pacing. Patients with a prolonged P wave on the ECG are thought to have intra-atrial conduction delay and atrial dyssynchrony.³⁵ In the present study, all patients had a prolonged P wave after conversion to sinus rhythm. P waves of the shortest duration were obtained after biatrial pacing compared with sinus rhythm, RAA pacing, and coronary sinus pacing. We suggest that intra-atrial resynchronisation by biatrial pacing may be important in producing the most improvement in atrial mechanical function compared with single site atrial pacing.

Clinical implications

Atrial mechanical stunning is thought to be one of the mechanisms responsible for the increased risk of thromboembolic complications after cardioversion of AF.^{5 6} Our findings suggest that atrial pacing just after cardioversion of persistent AF can potentially prevent subsequent thromboembolic complications. The observation that atrial pacing significantly reversed TMIF-A implicates an improvement in the haemodynamic function after cardioversion of AF. The finding that pacing rate may be an important factor in increasing atrial mechanical function may also have implications in the choice of post-cardioversion pacing rates in patients with implanted devices. The present study showed that biatrial pacing may be the best way to achieve these benefits. In clinical practice, biatrial pacing just after cardioversion of persistent AF from temporary leads inserted into the RAA and coronary sinus would be recommended.

Limitations

There are several limitations in the present study. Firstly, atrial pacing did not exceed 120 beats/min. In the clinical setting, we believe that atrial pacing over 120 beats/min may be inconvenient because patients often experience palpitation, decreased ventricular filling time, and impaired haemodynamic function in some patients, and may re-induce AF. Secondly, we could not evaluate the effects of the pacing rate on global left atrial function. Because the transmitral inflow pattern at 100 beats/min and 120 beats/min indicates a single fusion wave, consisting of both the early filling and atrial filling waves at all pacing sites, we could not evaluate TMIF-A at either 100 beats/min or 120 beats/min. Whether the effect of atrial pacing on global left atrial function has a positive force-frequency relation is still unknown. Thirdly, although we have shown the acute benefits of atrial pacing on atrial mechanical function just after electrical cardioversion of persistent AF, it remains unknown whether the improvement is sustained during continuous pacing over several weeks and whether the effects would remain over the time course of the recovery of atrial mechanical function. Unfortunately, at present, these are extremely limited because of the requirement for long term implanted devices. These may be important issues for further research.

Conclusion

Atrial pacing at increased rates can improve atrial mechanical function after cardioversion of persistent AF. Biatrial pacing might be the most effective technique to reverse atrial mechanical stunning.

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